

1           1. A method for diagnosing a malignant neoplasm in a  
2 mammal, comprising contacting a bodily fluid from said  
3 mammal with an antibody which binds to an human aspartyl  
4 (asparaginyl) beta-hydroxylase (HAAH) polypeptide under  
5 conditions sufficient to form an antigen-antibody complex  
6 and detecting the antigen-antibody complex.

1           2. The method of claim 1, wherein said neoplasm is  
2 derived from endodermal tissue.

1           3. The method of claim 1, wherein said neoplasm is  
2 selected from the group consisting of colon cancer, breast  
3 cancer, pancreatic cancer, liver cancer, and cancer of the  
4 bile ducts.

1           4. The method of claim 1, wherein said neoplasm is  
2 a cancer of the central nervous system (CNS).

1           5. The method of claim 1, wherein said bodily fluid  
2 is selected from the group consisting of a CNS-derived  
3 bodily fluid, blood, serum, urine, saliva, sputum, lung  
4 effusion, and ascites fluid.

1           6. The method of claim 1, wherein said antibody is a  
2 monoclonal antibody.

1           7. The method of claim 6, wherein said monoclonal  
2 antibody is FB50.

1           8. The method of claim 6, wherein said monoclonal  
2 antibody is selected from the group consisting of 5C7, 5E9,  
3 19B, 48A, 74A, 78A, 86A.

1           9. A method for prognosis of a malignant neoplasm  
2 of a mammal, comprising

3                 (a) contacting a bodily fluid from said mammal  
4 with an antibody which binds to an HAAH polypeptide under  
5 conditions sufficient to form an antigen-antibody complex  
6 and detecting the antigen-antibody complex;

7                 (b) quantitating the amount of complex to  
8 determine the level of HAAH in said fluid; and

9                 (c) comparing the level of HAAH in said fluid  
10 with a normal control level of HAAH, wherein increasing  
11 levels of HAAH over time indicates an adverse prognosis.

1           10. A method of inhibiting tumor growth in a mammal  
2 comprising administering to said mammal a compound which  
3 inhibits expression of HAAH.

1           11. The method of claim 10, wherein said compound is  
2 a HAAH antisense nucleic acid.

1           12. The method of claim 10, wherein said compound  
2 is a ribozyme.

1           13. The method of claim 10, wherein said tumor is  
2 derived from endodermal tissue.

1           14. The method of claim 10, wherein said tumor is  
2 selected from the group consisting of colon cancer, breast  
3 cancer, pancreatic cancer, liver cancer, and cancer of the  
4 bile ducts.

1           15. The method of claim 10, wherein said tumor is a  
2 CNS tumor.

1           16. A method of inhibiting tumor growth in a mammal  
2 comprising administering to said mammal a compound which  
3 inhibits an enzymatic activity of HAAH.

1           17. The method of claim 16, wherein said enzymatic  
2 activity is hydroxylase activity.

1           18. The method of claim 16, wherein said compound  
2 is a dominant negative mutant of HAAH.

1           19. The method of claim 18, wherein said dominant  
2 negative mutant HAAH comprises a mutation in a catalytic  
3 domain of HAAH.

1           20. The method of claim 16, wherein said compound  
2 is an HAAH-specific intrabody.

1           21. The method of claim 16, wherein said compound  
2 is L-mimosine.

1           22. The method of claim 16, wherein said compound  
2 is a hydroxypyridone.

1           23. A method of inhibiting tumor growth in a mammal  
2 comprising administering to said mammal a compound which  
3 inhibits signal transduction through the IRS signal  
4 transduction pathway.

1           24. The method of claim 23, wherein said compound  
2 inhibits IRS phosphorylation.

1           25. The method of claim 23, wherein said compound  
2 inhibits binding of Fos or Jun to an HAAH promoter sequence.

1           26. A method of inhibiting tumor growth in a mammal  
2 comprising administering to said mammal a compound which  
3 inhibits HAAH hydroxylation of a NOTCH polypeptide.

1           27. The method of claim 26, wherein said compound  
2 inhibits hydroxylation of an EGF-like repeat sequence in a  
3 NOTCH polypeptide.

1           28. A method of killing a tumor cell comprising  
2 contacting said tumor cell with cytotoxic agent linked to an  
3 HAAH-specific antibody.

1           29. A monoclonal antibody that binds to an epitope  
2 of HAAH.

1           30. The antibody of claim 29, wherein said epitope  
2 is within a catalytic site of HAAH.

1           31. The antibody of claim 29, wherein said  
2 monoclonal antibody is selected from the group consisting of  
3 5C7, 5E9, 19B, 48A, 74A, 78A, 86A.

1           32. The antibody of claim 29, wherein said  
2 monoclonal antibody is selected from the group consisting of  
3 HA238A, HA221, HA239, HA241, HA329, or HA355.

1           33. A composition comprising a monoclonal antibody  
2 that binds to an epitope of HAAH linked to a cytotoxic  
3 agent, wherein said composition preferentially kills tumor  
4 cells compared to non-tumor cells.

1           34. A kit for diagnosis of a tumor in a mammal,  
2 comprising the antibody of claim 29.

1           35. The kit of claim 34, wherein said antibody is  
2 immobilized on a solid phase.

1           36. The kit of claim 35, wherein said solid phase  
2 is selected from a group consisting of an assay plate, an  
3 assay well, a nitrocellulose membrane, a bead, a dipstick,  
4 and a component of an elution column.

1           37. A method of determining whether a candidate  
2 compound inhibits HAAH enzymatic activity, comprising  
3           (a) providing a HAAH polypeptide;  
4           (b) providing a polypeptide comprising an EGF-like  
5 domain;  
6           (c) contacting said HAAH polypeptide or said NOTCH  
7 polypeptide with said candidate compound;  
8           (d) determining hydroxylation of said polypeptide of  
9 step (b), wherein a decrease in hydroxylation in the  
10 presence of said candidate compound compared to that in the  
11 absence of said compound indicates that said compound  
12 inhibits HAAH enzymatic activity.

1           38. A method of determining whether a candidate  
2 compound inhibits HAAH activation of NOTCH, comprising  
3           (a) providing a cell expressing HAAH;  
4           (b) contacting said cell with a candidate compound;  
5 and  
6           (c) measuring translocation of activated NOTCH to  
7 the nucleus of said cell, wherein a decrease in  
8 translocation in the presence of said compound compared to  
9 that in the absence of said compound indicates that said  
10 compound HAAH activation of NOTCH.

a4d  
a2